Exhibit 159

Journal of Addictive Diseases, 30:185–194, 2011

ISSN: 1055-0887 print / 1545-0848 online
DOI: 10.1080/10550887.2011.581961

Routledge
Taylor & Francis Group

Prevalence of Prescription Opioid-Use Disorder Among Chronic Pain Patients: Comparison of the DSM-5 vs. DSM-4 Diagnostic Criteria

Joseph A. Boscarino, PhD, MPH
Margaret R. Rukstalis, MD
Stuart N. Hoffman, DO
John J. Han, MD
Porat M. Erlich, PhD, MPH
Stephen Ross, MD
Glenn S. Gerhard, MD
Walter F. Stewart, PhD, MPH

ABSTRACT. The authors estimated the prevalence of lifetime prescription opioid-use disorder among outpatients on opioid therapy using criteria from both versions 4 and 5 of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM). Using electronic records from a large health care system, a random sample of outpatients undergoing long-term opioid therapy for non-cancer pain was identified and 705 participants completed diagnostic interviews. The prevalence of lifetime DSM-5 opioid-use disorder among these patients was 34.9% (95% confidence interval [CI] = 30.5–39.5), similar to the prevalence of DSM-4 opioid dependence (35.5%, 95% CI = 31.1–40.2). The Kappa value between DSM-5 and

Joseph A. Boscarino is affiliated with the Center for Health Research, Geisinger Clinic, Danville, PA, Department of Medicine & Pediatrics, Mount Sinai School of Medicine, New York, NY, and the Department of Psychiatry, Temple University School of Medicine, Philadelphia, PA. Margaret R. Rukstalis is affiliated with the Center for Health Research, Geisinger Clinic, Danville, PA. Stuart N. Hoffman and John J. Han are affiliated with the Department of Pain Medicine, Geisinger Clinic, Danville, PA. Porat M. Erlich is affiliated with the Center for Health Research, Geisinger Clinic, Danville, PA, and Department of Medicine, Temple University School of Medicine, Philadelphia, PA. Stephen Ross is affiliated with the Department of Psychiatry, NYU Langone School of Medicine, New York, NY. Glenn S. Gerhard is affiliated with the Weis Center for Research, Geisinger Clinic, Danville, PA. Walter F. Stewart is affiliated with the Center for Health Research, Geisinger Clinic, Danville, PA, and the Johns Hopkins Bloomberg School of Public Health, Baltimore, MD.

Address correspondence to: Joseph A. Boscarino, PhD, MPH, Senior Investigator, Center for Health Research, Geisinger Clinic, 100 N. Academy Avenue, Danville, PA 17822-4400 (E-mail: jaboscarino@geisinger.edu).

Preliminary results from this study were presented at the 15th Annual HMO Research Network Conference, Danville, PA, April 2009.

Funding for this study was by a grant from the Administrative Committee for Research (ACR), Geisinger Clinic, Grant No. TRA-015 (Dr. Boscarino, PI). The ACR had no role in study design, data collection, analysis, interpretation, writing, or in the decision to submit the manuscript for publication.

DSM-4 criteria was high (Kappa = 0.873, $p < 0.0001$). Logistic regressions suggested DSM-5 opioid-use disorder was associated with age younger than 65 (odds ratio [OR] = 2.25, $p = 0.009$), history of opioid abuse (OR = 4.94, $p < 0.001$), higher opioid withdrawal symptoms (OR = 3.01, $p = 0.008$), and history of substance abuse treatment (OR = 1.62, $p = 0.015$), similar to DSM-4. Based on DSM-5, 21.7% of patients met criteria for moderate and 13.2% for severe opioid-use disorder, respectively. Given the changes proposed, the finding that the prevalence of and risk factors for DSM-5 opioid-use disorders were similar to DSM-4 were unexpected. Further research is advised.

KEYWORDS. Opioids, drug-use disorder, DSM-5, DSM-4, prescription drugs, pain, outpatients

INTRODUCTION

The proposed diagnostic criteria for the *Diagnostic and Statistical Manual of Mental Disorders,* fifth edition (DSM-5) includes modifications for prescription opioid-use disorders.[1,2] These include elimination of the tolerance and withdrawal symptoms used in DSM-4.[3] The rationale for the latter is that these symptoms would likely be "iatrogenic" rather than psychopathogenic within a therapeutic context.[4] In addition, given the issues noted with the DSM-4 distinction between *abuse* and *dependence*, the recommendation has been to combine these symptoms into a single disorder of graded severity.[3] Given these proposed changes, the objectives of the current study are threefold: to assess the prevalence of DSM-5 prescription opioid-use disorder among an at-risk population, to identify key risk factors associated with this new classification system; and to compare DSM-5 criteria with DSM-4 criteria to better direct future research efforts.

METHODS

Study Sample

As described elsewhere,[5] individuals for this study were randomly selected from primary and specialty care outpatients seen in the Geisinger Clinic, which is a part of the Geisinger Health System, an integrated system that serves residents in 31 central and northeastern Pennsylvania counties. Patients were eligible for this study if they were 18 years of age or older, received care from one of nine community practice clinics or from the three specialty clinics, and were prescribed opioid medications for non-malignant pain four or more times in a 12-month period (mean prescriptions = 10.72, standard deviation [SD] = 4.96) This study was approved by the Geisinger Health System Institutional Review Board.

Data Collection

Telephone interviews were completed from August 2007 through November 2008. Following patient notification letters, telephone recruitment was initiated. A total of 2,373 patients were contacted by telephone to complete a patient survey. Of these patients, 234 were determined to be ineligible for study due to death, institutionalization, language barriers, illness, denial of opioid use, or due to being in the last survey batch (n = 79) not contacted because the study quota was completed. Our survey completion rate was 33% (705 of 2,139) and our survey cooperation rate (i.e., percentage interviewed after patient contact) was 51% (705 of 1,390).[5]

Following patient consent, interviewers administered structured diagnostic interviews that also included (1) a modified Composite International Diagnostic Interview (CIDI),[6] (2) assessment of depression, post-traumatic stress disorder (PTSD), general anxiety, and psychological trauma using a diagnostic interview designed for this purpose,[7–9] and (3) questions relevant to opioid dependence severity,[10] tobacco dependence,[11,12] and childhood adversity.[13,14] We examined these different clinical domains because we wanted to determine key factors to predict substance dependence in clinical practice.[15] The survey was administered using a computer-assisted telephone interviewing (CATI) system.

All interviewers received extensive training in the administration of these diagnostic interviews and were under the direct supervision of experienced research staff. The interviews were conducted at the Center for Health Research's Survey Center located at Geisiner Clinic's main campus in Danville, Pennsylvania.

DSM-4 and DSM-5 Substance Misuse

For the current study, *substance misuse* was defined based on both the DSM-4 criteria for dependence and the proposed DSM-5 criteria for drug-use disorder.[16, 17] Because we assessed prescription opioid dependence at the beginning of the interview, we used a substance dependence scale adapted for telephone administration that had been previously validated.[18, 19] The criteria for dependence on this scale were concordant with standard DSM nomenclature.[16] History of DSM-4 prescription opioid abuse was defined in the study as the presence of one or more prescription opioid abuse problems (e.g., health, family, functional, or legal problems) in the patient's history. Consistent with the proposed DSM-5 criteria for prescription opioid-use disorder,[17] we counted the occurrence of opioid dependence symptoms but excluded those for tolerance and withdrawal.[4] We also included one opioid craving symptom and three prescription opioid abuse symptoms in this count, as currently proposed in DSM-5.[17] For both the DSM-5 and DSM-4 lifetime estimates, and consistent with these respective criteria, these symptom clusters had to occur within the same 12-month period. The DSM-5 classification also included the proposed severity classification, whereby patients having 2 to 3 symptoms were classified as having moderate and those having 4 or more symptoms were classified as severe opioid-use disorder, respectively. Finally, although current prescription opioid-use disorder estimates (i.e., past 12 months) were not available for DSM-5 in this study, these were reported previously for DSM-4 prescription opioid dependence among these patients.[5]

Nicotine and Alcohol Dependence

The Fagerstrom Tolerance Scale (FTS) was used to assess nicotine dependence.[11, 12] We used the diagnostic cut-off point for this scale, defined as a score of 7 or higher.[11] The FTS has good concurrent and predictive validity for nicotine dependence and has been widely used in research.[20] Alcohol dependence was assessed using the CIDI instrument based on DSM-4 criteria.[6]

Mental Health Disorders, Pain, and Trauma

Because our other study measures were discussed elsewhere,[5] we only briefly review them here. Major depression was assessed using a depression measure developed from the *Structured Clinical Interview for DSM-IV* instrument,[21] and validated in other telephone surveys.[7,22,23] PTSD was based on the DSM-4 and developed for telephone administration, as used in previous trauma studies.[7,23, 24] We used the Brief Pain Inventory (BPI) to assess current pain status in the past 7 days.[25, 26] The BPI is a widely used scale and is often used to assess chronic, nonmalignant pain. Trauma exposure was assessed using a history of childhood adversity and a lifetime trauma exposure scale, respectively. Childhood adversity was assessed using a scale developed by Felitti et al.[13, 14] This scale has been previously validated.[27, 28] For lifetime trauma exposure, we used a measure that focused on major traumatic events experienced (e.g., forced sexual contact, being attacked with a weapon) and that occurred prior to the interview. This scale has been used and validated in previous studies.[7,9,2123]

Other Measures

Other measures included history of substance abuse treatments, history of psychiatric care, current psychotropic medication use, history of illicit drug use (e.g., amphetamines, marijuana, cocaine), and self-reported health status. Our study also included the Severity of Dependence Scale (SDS), adopted for prescription opioids.[10] The SDS has been used in addiction research and previously validated.[29] This scale is considered to be a good measure of withdrawal symptoms.[30] We used a score of 7 or higher to define high lifetime opioid withdrawal severity.[31]

Statistical Analyses

We analyzed patient selection bias using electronic health record data to compare study respondents ($n = 705$) to non-respondents ($n = 1434$). We then used these results to develop weights to adjust for potential selection bias. We also completed point estimates for DSM-5 opioid-use disorder (with 95% confidence intervals) and compared these with DSM-4 opioid dependence. Following this, we examined descriptive statistics for DSM-5 prescription opioid-use disorder by demographic and risk factor characteristics. Next, we completed logistic regressions to identify risk-factors for DSM-5 opioid-use disorder. To identify robust multivariate models and prevent model over-fitting, only variables with bivariate p values < 0.10 were selected as candidate measures. In addition, only variables that remained significant were retained in the final models. Ordinal regression was also used to assess risk factors for the severity of DSM-5 opioid-use disorder.[31] We also compared bivariate/multivariate results for DSM-5 to those previously reported for DSM-4.[5] Finally, because these patients were clustered within 12 clinics, we used the survey data module in Stata version 11.1 to adjust for patient clustering in all analyses.[32]

RESULTS

Analyses suggested that study non-participants tended to be men, unmarried, current smokers, seen in primary care clinics, and less ill than study participants ($p < 0.05$). However, no differences were found in participation rates by race, employment status, obesity status, or the number of prescriptions received for opioids in the past 3 years. Based on these results, case weights were developed to adjust for differences in participation by gender and clinic setting, and these weights were used in subsequent analyses.

As shown in Table 1, 34.9% (95% confidence interval [CI] = 30.5–39.5) of longer-term opioid users, defined as those who received 4 or more prescriptions in the past 12 months (mean = 10.72, SD = 4.96), meet DSM-5 criteria for lifetime prescription opioid-use disorder. In addition, 35.5% (95% CI = 31.1–40.2) of these patients meet criteria for prescription for DSM-4 opioid dependence. Results for the proposed DSM-5 severity criteria suggest that 21.7% (95% CI = 18.7–25.1) of patients have moderate drug-use disorder and 13.2% (95% CI = 9.8–17.6) have severe drug-use disorder (Table 1). Noteworthy is that the overlap between DSM-5 and DSM-4 is substantial (Kappa = 0.873, $p < 0.0001$) (Table 1). As can be seen, 92% of those with a DSM-5 opioid-use disorder also meet the criteria for DSM-4 opioid dependence, and 95% of those without a DSM-5 opioid-use disorder do not meet the criteria for DSM-4 opioid dependence (Table 1).

Lifetime opioid-use disorder was associated with age younger than 65 years ($p < 0.001$), reporting poorer health status ($p < 0.01$), and reporting higher average pain levels ($p < 0.05$) and pain impairment ($p < 0.01$) (Table 2). Those who meet lifetime criteria for opioid abuse were more likely to meet lifetime criteria for opioid-use disorder ($p < 0.001$) (Table 3). Also, those with a history of higher opioid withdrawal symptoms also had a higher prevalence of opioid-use disorder ($p < 0.001$). Lifetime opioid-use disorder was also associated with lifetime alcohol dependence ($p < 0.01$), tobacco dependence ($p < 0.01$), major depression ($p < 0.001$), generalized anxiety disorder ($p < 0.001$), and lifetime PTSD ($p < 0.001$). Those with lifetime opioid-use disorder also had a history of childhood adversity ($p < 0.001$), exposure to psychological trauma ($p < 0.001$), illicit drug use ($p < 0.001$), substance abuse treatment ($p < 0.001$), recent psychotropic medication use ($p < 0.001$), and a history of antisocial personality disorder ($p < 0.001$) (Table 3).

Based on these bivariate results, two multivariate logistic models were developed for opioid-use disorder—one without opioid abuse as a predictor (model 1) and one with opioid abuse (model 2). We did this because the DSM-5 drug abuse symptoms are now included in the diagnostic symptom count. Using the selection criteria discussed above, six predictor variables were identified for inclusion in model 1. For this model, DSM-5 opioid-use disorder was associated with age older than 65 ($p < 0.004$),

TABLE 1. Prevalence of Lifetime DSM-5 Prescription Opioid-Use Disorder by Lifetime DSM-4 Prescription Opioid Dependence[a]

	DSM-5 Opioid-Use Disorder						Total DSM-4 Opioid Dependence		
	Not Present			Present			Present		
Diagnostic Criteria Used*	%	95% CI	(n)	%	95% CI	(n)	%	95% CI	(n)
DSM-4 opioid dependence not present	94.9	92.2–96.7	(436)	7.7	4.3–13.4	(18)	64.5	59.8–68.9	(454)
DSM-4 opioid dependence present	5.1	3.3–7.8	(23)	92.3	86.6–95.7	(228)	35.5	31.1–40.2	(251)
Total DSM-5 opioid-use disorder[b]	65.1	60.5–69.5	(459)	34.9	30.5–39.5	(246)	100.0	–	(705)

Note: The first panel shows DSM-5 opioid-use disorder by DSM-4 opioid dependence; the panel on the far right shows the prevalence of DSM-4 opioid dependence only.
[a]All percent results adjusted/weighted for response bias and data clustering, Ns are unweighted.
[b]Moderate opioid-use disorder: 2 to 3 criteria = 21.7% (95% CI = 18.7–25.1); severe opioid-use disorder: 4 or more criteria = 13.2% (95% CI = 9.8–17.6).
*Kappa = 0.873, $p < 0.0001$.

TABLE 2. Demographic and Health Characteristics of Patients Meeting DSM-5 Criteria for Lifetime Prescription Opioid-Use Disorder[a]

Study Variables	Total Sample Percent (n)	Opioid-Use Disorder Percent (n)	No Opioid-Use Disorder Percent (n)
Age			
18–64 years old[b]	79.3 (558)	90.9 (223)	73.1 (335)***
65+ Years Old	20.7 (147)	9.1 (23)	26.9 (124)
Gender			
Male	39.1 (232)	40.6 (85)	38.3 (147)
Female	60.9 (473)	59.4 (164)	61.7 (312)
Race			
White	98.4 (694)	97.7 (241)	98.8 (453)
Non-White	1.6 (11)	2.3 (5)	1.2 (6)
Marital status			
Married	65.6 (458)	62.3 (151)	66.4 (307)
Not married	34.4 (247)	37.7 (95)	33.6 (152)
Employment status			
Employed	25.7 (179)	21.9 (53)	27.7 (126)
Not employed	74.3 (526)	78.1 (193)	72.3 (333)
Household income			
Less than $30,000 per year	41.0 (289)	43.7 (109)	39.5 (180)
Greater than $30,000 per year	46.3 (326)	46.2 (111)	46.4 (215)
Refused to provide income	12.7 (90)	10.1 (26)	14.1 (64)
Education			
High school or less	50.2 (351)	49.0 (120)	50.9 (231)
Some college or more	49.8 (352)	51.0 (126)	49.1 (226)
Clinic setting			
Primary care	83.1 (563)	81.1 (191)	84.2 (372)
Specialty clinic	16.9 (142)	18.9 (55)	15.8 (87)
Reported health status			
Good	80.8 (570)	71.0 (176)	86.0 (394)**
Fair/poor	19.2 (135)	29.0 (70)	14.0 (65)
Medically obese (BMI > 30)			
Yes	50.3 (353)	47.0 (116)	52.0 (237)
No	49.7 (352)	53.0 (130)	48.0 (222)
Reported average pain in past week			
High	23.8 (173)	29.4 (75)	20.7 (98)*
Not high	76.2 (532)	70.6 (171)	79.3 (361)
Reported pain currently interfered with life or work – greatly or extremely			
Yes	60.4 (426)	72.5 (178)	53.9 (248)**
No	39.6 (279)	27.5 (68)	46.1 (211)
Total	**705**	**246**	**459**

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

[a]All percent results adjusted/weighted for response bias and data clustering, Ns are unweighted.

[b]It is noted that age is collapsed as shown due to the lower prevalence of opioid dependence among those 65 years of age and older. As seen in Table 3, of those with lifetime prescription opioid-use disorder, ~ 91% are less than 65 years old. The mean age of the study population was 54.55 (95% CI = 50.2–58.9).

history of high opioid withdrawal symptoms ($p < 0.001$), history of substance abuse treatment ($p < 0.003$), history of antisocial personality disorder ($p = 0.038$), current pain impairment ($p = 0.023$), and history of major depression ($p = 0.007$). The logistic model that included opioid abuse as a predictor (model 2) was similar, except that pain interference and major depression did not meet criteria for inclusion (analyses available on request).

Because DSM-5 also proposed opioid-use disorder severity classifications, including the presence of moderate disorder (2 to 3 symptoms) and severe disorder (4 or more

TABLE 3. Mental Health Characteristics of Patients Meeting DSM-5 Criteria for Lifetime Prescription Opioid-Use Disorder[a]

Study Variables	Total Sample Percent (n)	Lifetime DSM-5 Opioid-Use Disorder Percent (n)	No Lifetime DSM-5 Opioid-Use Disorder Percent (n)
Lifetime history of prescription opioid abuse			
Yes	32.8 (230)	61.1 (151)	17.6 (79)***
No	67.2 (475)	38.9 (95)	82.4 (380)
High prescription opioid withdrawal severity			
Yes	15.0 (108)	30.3 (77)	6.9 (31)***
No	85.0 (597)	69.7 (169)	93.1 (428)
Lifetime alcohol dependence			
Yes	9.8 (68)	14.8 (37)	7.1 (31)**
No	90.2 (637)	85.2 (209)	92.9 (428)
Lifetime tobacco dependence			
Yes	36.8 (251)	42.7 (101)	33.7 (150)**
No	63.2 (454)	57.3 (145)	66.3 (309)
Lifetime major depressive disorder			
Yes	34.6 (249)	51.0 (128)	25.8 (121)***
No	65.4 (456)	49.0 (118)	74.2 (338)
Lifetime generalized anxiety disorder			
Yes	12.6 (89)	21.4 (52)	7.9 (37)***
No	87.4 (616)	78.6 (194)	92.1 (422)
Lifetime posttraumatic stress disorder			
Yes	13.3 (97)	20.5 (51)	9.4 (46)***
No	86.7 (608)	79.5 (195)	90.6 (413)
History of high childhood adversity			
Yes	24.9 (178)	34.7 (86)	19.6 (92)***
No	75.1 (527)	65.3 (160)	80.4 (367)
History of high exposure to psych trauma			
Yes	23.0 (161)	33.9 (83)	17.1 (78)***
No	77.0 (544)	66.1 (163)	82.9 (381)
History of illicit drug use			
Yes	39.3 (273)	50.0 (122)	33.6 (151)***
No	60.7 (432)	50.0 (124)	66.4 (308)
History of substance abuse treatment			
Yes	22.5 (153)	37.5 (90)	14.5 (63)***
No	77.5 (552)	62.5 (156)	85.5 (396)
Current psychotropic medication use			
Yes	61.1 (434)	70.6 (176)	56.0 (258)***
No	38.9 (271)	29.4 (70)	44.0 (201)
Anti-social personality disorder			
Yes	23.8 (167)	33.9 (84)	18.4 (83)***
No	76.2 (538)	66.1 (162)	81.7 (376)
Total	**705**	**246**	**459**

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

[a]All percent results adjusted/weighted for response bias and data clustering, Ns are unweighted.

symptoms), we also used multivariate ordinal regression to examine our results (Table 4). As can be seen, the best predictors of higher opioid-use disorder severity are age younger than 65 years, history of opioid abuse, history of high opioid withdrawal symptoms, and history of substance abuse treatment (p values < 0.0001). The risk factors for severe opioid-use disorder stand out from moderate opioid-use disorder. Noteworthy is that patients with a history of abuse are much more likely to have more severe opioid-use disorder (OR = 6.07), compared with those who do not meet criteria for opioid abuse (Table 4). Higher severity is also associated with prescription psychotropic medications use. Interestingly, history of illicit drug use appears to be

TABLE 4. Ordinal Regression Model Predicting Severity of Lifetime DSM-5 Opioid-Use Disorder[a] ($N = 705$)

Predictor Variables[b]	OR	95% CI	p
Less than 65 years old	2.70	1.68–4.32	< 0.0001
History of high severity on SDS	3.43	2.29–5.14	< 0.0001
Substance abuse treatment	1.93	1.51–2.48	< 0.0001
Positive for anti-social personality	1.61	1.19–2.17	0.002
History of opioid abuse	6.07	4.05–9.08	< 0.0001
History of illicit drug use	0.75	0.59–0.96	0.021
Currently prescribed psychotropic drugs	1.53	1.08–2.18	0.016
Cut 1	2.72	2.12–3.32	–
Cut 2	4.50	3.64–5.35	–

[a]All results adjusted/weighted for response bias and data clustering.
[b]Adjusted-pseudo $R^2 = 0.205$ for entire model.
OR = odds ratio; SDS = severity of dependence scale.
Ordinal contrasts for regression model include no opioid-use disorder ($n = 459$); moderate opioid-use disorder ($n = 153$); severe opioid-use disorder ($n = 93$).

protective for severe opioid-use disorder (OR = 0.75, $p = 0.021$).

DISCUSSION

Our study suggests that as many as 35% (95% CI = 30.5–39.5) of the patients undergoing longer-term opioid therapy meet criteria for lifetime prescription opioid-use disorder based on the proposed DSM-5 criteria. This is approximately the same percent that meet DSM-4 criteria for opioid dependence (Table 1). The Kappa coefficient for those meeting DSM-5 and DSM-4 concurrently was high (Kappa = 0.873, $p <$ 0.0001), suggesting considerable clinical overlap. This finding is surprising, given the differences between these diagnostic criteria. For DSM-5, the proposed criteria for prescription opioid-use disorder exclude withdrawal and tolerance symptoms, which could be considered "iatrogenic" under medical supervision.[4] In addition, drug abuse-related problems (e.g., work, family, health, and legal problems) have been added to the DSM-5 symptom count, as was a symptom related to drug craving. Furthermore, only two positive symptoms are required to qualify for opioid-use disorder. Finally, a severity classification has been added to the diagnostic nomenclature, with the presence of 2 to 3 symptoms classified as "moderate" and 4 or more symptoms classified as "severe" opioid-use disorder. By comparison, for DSM-4 opioid dependence, only the drug dependence symptoms are counted, including withdrawal and tolerance symptoms, with 3 or more symptoms required to meet criteria.

The DSM-5 changes proposed were expected to have an effect, especially because prescription opioid dependence estimates that included these withdrawal and tolerance symptoms were thought to be too high.[33] As demonstrated, this was not the case. Examination of specific symptoms by DSM-5 status suggested why this phenomenon occurred: those cases that would have been excluded under DSM-5 due to elimination of withdrawal and tolerance symptoms were now included not only by the addition of the drug abuse and drug craving symptoms, but also by retention of "loss of control" symptoms in DSM-5. This is because those with withdrawal and tolerance symptoms under DSM-4 opioid dependence criteria also have these other symptoms under DSM-5.

In bivariate analyses, being younger, reporting poorer health, having higher average pain, and reporting higher pain impairment were associated with DSM-5 opioid-use disorder (Table 2), as was having a history of opioid abuse and higher opioid withdrawal symptom severity (Table 3). Lifetime DSM-5 opioid-use disorder was also associated with lifetime alcohol dependence, tobacco dependence, major depression, generalized anxiety disorder,

lifetime PTSD, history of childhood adversity, exposure to psychological trauma, illicit drug use, substance abuse treatment, psychotropic medication use, and a history of anti-social personality disorder (Table 3). Noteworthy is that these are essentially the same risk factors previously reported for DSM-4 opioid dependence.[31]

In multivariate logistic analyses, the risk factors for DSM-5 opioid-use disorder include younger age, as well as history of higher opioid withdrawal severity, substance abuse treatment, antisocial personality disorder, and history of major depression. Higher current pain impairment is also significant. The logistic model that included opioid abuse as a predictor was similar, except that pain interference and major depression did not meet criteria for inclusion in this model. As was seen, using ordinal regression, the best predictors of opioid-use disorder severity were age less than 65, history of opioid abuse, history of high opioid withdrawal severity, and history of substance abuse treatment. Noteworthy is that patients with a history of opioid abuse are six times more likely to have higher opioid-use disorder severity (OR = 6.07), compared with those who do not meet these abuse criteria. Higher severity is also associated with current psychotropic medications use. Interestingly, history of illicit drug use appears to be protective of higher severity of opioid-use disorder, warranting further investigation. It is noted that the multivariate risk factors for DSM-5 prescription opioid-use disorder are essentially the same as reported previously for DSM-4 opioid dependence.[31] Given the changes proposed for DSM-5, again, this was unexpected.

This study has strengths and limitations.[5] Study strengths include that this research was based on a random sample of outpatients seen in a large multi-specialty group practice; that drug-use disorder was assessed based on DSM criteria; and that participants were identified through drug orders in the electronic health record, not patient self-report or treatment records. Study limitations include that our diagnostic data were based on patient self-report; that our survey completion rate was less than optimal; and that our patients were drawn from a predominately Caucasian population in one geographic region of the United States. Another limitation was that we could not compare DSM-5 status for current opioid-use disorder (i.e., past 12 months) because we did not have the latter information in our survey data. However, we did report the detailed DSM-4 results for current opioid dependence elsewhere.[5] There is no reason to expect that the findings for current opioid-use disorder for DSM-5 would be substantially different than lifetime opioid-use disorder reported in this study, other than the former would be lower prevalence than the latter.[5]

To our knowledge, this is the first study to compare DSM-5 to DSM-4 for prescription opioid misuse and to report results for DSM-5 moderate and severe opioid-use disorder. We did not expect that the prevalence of and risk factors for the DSM-5 and DSM-4 would be essentially the same given the proposed changes. As discussed, the reason for this is that different symptoms now qualify the same patients for inclusion who would have been excluded under the alternative classification system and that the loss of control symptoms retained in DSM-5 are collinear with tolerance and withdrawal symptoms. Our plan is to replicate these findings and to further investigate the biologic and genetic correlates of the proposed DSM-5 criteria.[30] Perhaps then we might better validate the neurobiological bases of these diagnostic classifications,[34] which was a rationale for the DSM diagnostic nomenclature in the first place.[1,17] Further clinical and epidemiological research is urged to clarify and expand these findings.

REFERENCES

1. Regier DA, Narrow WE, Kuhl EA, Kupfer DJ. The conceptual development of DSM-V. Am J Psychiatry 2009; 166:645–50.

2. Pierre JM. A psychiatry of tomorrow: DSM-5 and beyond. Psychiatric Times 2010; 27(June 25). http://www.psychiatrictimes.com/blog/couchincrisis/content/article/10168/1598800. Accessed January 5, 2011.

3. King SA. DSM-5 and pain. Psychiatric Times 2010; 27 (February 7). http://www.psychiatrictimes.com/display/article/10168/1494500. Accessed January 5, 2011.

4. O'Brien CP, Volkow N, Li TK. What's in a word? Addiction versus dependence in DSM-V. Am J Psychiatry 2006; 163:764–5.

5. Boscarino JA, Rukstalis M, Hoffman SN, et al. Risk factors for drug dependence among out-patients on opioid

therapy in a large US health-care system. Addiction 2010; 105:1776–82.

6. Kessler RC, Ustun TB. The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). Int J Methods Psychiatr Res 2004; 13: 93–121.

7. Boscarino JA, Adams RE. Overview of findings from the World Trade Center Disaster Outcome Study: Recommendations for future research after exposure to psychological trauma. Int J Emerg Ment Health 2008; 10:275–90.

8. Boscarino JA, Adams RE. Peritraumatic panic attacks and health outcomes two years after psychological trauma: Implications for intervention and research. Psychiatry Res 2009; 167:139–50.

9. Boscarino JA, Adams RE. PTSD onset and course following the World Trade Center disaster: Findings and implications for future research. Soc Psychiatry Psychiatr Epidemiol 2009; 44:887–98.

10. Gossop M, Darke S, Griffiths P, et al. The Severity of Dependence Scale (SDS): Psychometric properties of the SDS in English and Australian samples of heroin, cocaine and amphetamine users. Addiction 1995; 90:607–14.

11. Fagerstrom KO. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict Behav 1978; 3:235–41.

12. Heatherton TF, Kozlowski LT, Frecker RC, Fagerstrom KO. The Fagerstrom test for nicotine dependence: A revision of the Fagerstrom Tolerance Questionnaire. Br J Addict 1991; 86:1119–27.

13. Dong M, Giles WH, Felitti VJ, et al. Insights into causal pathways for ischemic heart disease: Adverse Childhood experiences study. Circulation 2004; 110:1761–6.

14. Felitti VJ, Anda RF, Nordenberg D, et al. Relationship of childhood abuse and household dysfunction to many of the leading causes of death in adults. The Adverse Childhood Experiences (ACE) study. Am J Prev Med 1998; 14:245–58.

15. Kessler RC, Wang PS. The descriptive epidemiology of commonly occurring mental disorders in the United States. Ann Rev Public Health 2008; 29:115–29.

16. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fourth Text Revision ed. Arlington, VA: American Psychiatric Publishing, 2000.

17. American Psychiatric Association. *DSM-5: Opioid-use disorder*. http://www.dsm5.org/ProposedRevisions/Pages/proposedrevision.aspx?rid=460. Accessed September 16, 2010.

18. Hanson RF, Self-Brown S, Fricker-Elhai A, Kilpatrick DG, Saunders BE, Resnick H. Relations among parental substance use, violence exposure and mental health: The national survey of adolescents. Addict Behav 2006; 31:1988–2001.

19. Kilpatrick DG, Ruggiero KJ, Acierno R, Saunders BE, Resnick HS, Best CL. Violence and risk of PTSD, major depression, substance abuse/dependence, and comorbidity: Results from the National Survey of Adolescents. J Consult Clin Psychol 2003; 71:692–700.

20. Fagerstrom KO, Schneider NG. Measuring nicotine dependence: A review of the Fagerstrom Tolerance Questionnaire. J Behav Med. 1989; 12:159–82.

21. Boscarino JA, Adams RE, Figley CR. Mental health service use 1-year after the World Trade Center disaster: Implications for mental health care. Gen Hosp Psychiatry 2004; 26:346–58.

22. Acierno R, Kilpatrick DG, Resnick H, Saunders B, De Arellano M, Best C. Assault, PTSD, family substance use, and depression as risk factors for cigarette use in youth: Findings from the National Survey of Adolescents. J Trauma Stress 2000; 13:381–96.

23. Galea S, Ahern J, Resnick H, et al. Psychological sequelae of the September 11 terrorist attacks in New York City. N Engl J Med 2002; 346:982–7.

24. Boscarino JA, Adams RE, Figley CR. Worker productivity and outpatient service use after the September 11th attacks: Results from the New York City terrorism outcome study. Am J Ind Med 2006; 49:670–82.

25. Cleeland CS, Ryan KM. Pain assessment: Global use of the Brief Pain Inventory. Ann Acad Med Singapore 1994; 23:129–38.

26. Tan G, Jensen MP, Thornby JI, Shanti BF. Validation of the Brief Pain Inventory for chronic nonmalignant pain. J Pain 2004; 5:133–7.

27. Chapman DP, Whitfield CL, Felitti VJ, Dube SR, Edwards VJ, Anda RF. Adverse Childhood Experiences and the risk of depressive disorders in adulthood. J Affect Disord 2004; 82:217–25.

28. Flaherty EG, Thompson R, Litrownik AJ, et al. Effect of early childhood adversity on child health. Arch Pediatr Adolesc Med 2006; 160:1232–8.

29. Gossop M, Best D, Marsden J, Strang J. Test-retest reliability of the Severity of Dependence Scale. Addiction 1997; 92:353.

30. Erlich PM, Hoffman SN, Rukstalis M, et al. Nicotinic acetylcholine receptor genes on chromosome 15q25.1 are associated with nicotine and opioid dependence severity. Hum Genet 2010; 128:491–9.

31. Long JS, Freese J. Regression Models for Categorical Dependent Variables using Stata. 2nd ed. College Station, TX: Stata Press, 2006.

32. Stata Corporation. Stata, version 11.1. College Station, TX, 2010.

33. Von Korff M.Commentary on Boscarino et al. (2010): Understanding the spectrum of opioid abuse, misuse and harms among chronic opioid therapy patients. Addiction 2010; 105:1783–4.

34. Saunders JB, Schuckit MA, Sirovatka PJ, Regier DA, eds. Diagnostic issues in substance use disorders: Refining the Research Agenda for DSM-5. Arlington, VA: American Psychiatric Association, 2007.